UNITED STATES DISTRICT COURT
DISTRICT OF NEW HAMPSHIRE

LISA D. CARPENTER and JEFFREY D. CARPENTER, Plaintiff, vs. ELI LILLY AND COMPANY, an Indiana corporation, Defendant.	Civil Action No. 1:14-CV-00540-PB Hon. Paul J. Barbadoro **OPPOSITION TO DEFENDANT ELI LILLY'S MOTION FOR JUDGMENT ON THE PLEADINGS UNDER FED. R. CIV. P. 12(c)**

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INTRODUCTION

Federal drug regulation is designed to protect consumers. There is, however, only so much the Food and Drug Administration ("FDA") can do. "[T]he FDA has limited resources to monitor the 11,000 drugs on the market," so Congress looks to the enforcement of state law to complement federal regulation. *Wyeth v. Levine*, 555 U.S. 555, 578-79 (2009). State law provides a backstop. This is why Congress never amended the Food, Drug, and Cosmetic Act ("FDCA") to limit private actions against pharmaceutical companies. *Id.* at 570. The Supreme Court explains that "through many amendments to the FDCA and to FDA regulations, it has remained a central premise of federal drug regulation that the manufacturer bears responsibility for the content of its label at all times. It is charged both with crafting an adequate label and with ensuring that its warnings remain adequate as long as the drug is on the market." *Id.*

Within this legal framework, Defendant Eli Lilly and Company ("Lilly") moves for judgment on the pleadings. Plaintiffs allege that "Lilly's promotional campaigns have continuously failed to provide adequate instructions to users and health care professionals for stopping Cymbalta and have failed to include adequate warnings that fully and accurately inform users and health care professionals about the frequency, severity, and/or duration of Cymbalta withdrawal." (Complaint ("Compl.") ¶ 14.) Plaintiffs also allege that Cymbalta was defectively designed because it is impossible to safely taper off Cymbalta below 20 mg. (*Id.* ¶ 19.) Lilly argues that it cannot be liable under New Hampshire law for misrepresenting and omitting important safety information in its marketing of the antidepressant Cymbalta, or for failing to design a safer dosing regimen, because complying with New Hampshire law on these points would result in Lilly violating federal law. In other words, Lilly claims there is a conflict between the requirements of New Hampshire and federal law and, because of the Supremacy Clause, New Hampshire law is preempted.

On its face, this argument seems implausible. And, it should. The Supreme Court holds that

there is a strong presumption *against* state law being preempted unless the party asserting preemption can show a clear conflict of law. *Bates v. Dow Agrosciences LLC*, 544 U.S. 431, 449 (2005); *Geier v. Am. Honda Motor Co., Inc.*, 529 U.S. 861, 885 (2000).

With regard to Plaintiffs' failure to warn claims, Lilly tries to overcome this presumption by arguing that: (1) the Plaintiffs' allegations are based on a misleading label; (2) the only way Lilly could have changed the Cymbalta label was to use a regulation that requires Lilly to base a label change on "newly acquired information;" and (3) Plaintiffs' Complaint does not allege newly acquired information. This argument, however, makes two flawed assumptions.

First, Lilly assumes this case is only about a misleading label. It is not. The allegations in the Complaint specifically allege Lilly's overall marketing of Cymbalta was improper. (*E.g.*, Compl. ¶ 14.) The Complaint alleges that Lilly could have complied with its obligations under New Hampshire law and "relayed these instructions and warnings through the same means it utilized to promote its products, which included but are not limited to its labeling, 'Dear Doctor letters,' advertisements, and sales representatives." (Compl. ¶ 26.) Lilly's impossibility argument is narrowly focused on whether Lilly could have made changes to the Cymbalta warning label and, thus, completely ignores the other ways Lilly could have complied with New Hampshire law without running afoul of federal regulation. There is no impossibility.

Second, even if this lawsuit were strictly limited to Lilly's use of a misleading label, Lilly's claim that the Complaint alleges no "newly acquired information" is wrong. The Complaint discusses, at length, a publication by Dr. David Perahia—an employee of Lilly—in 2005 (post-approval) that discusses and makes recommendations about clinical trial data he evaluated as part of a larger meta-analysis. This reanalysis is, even under Lilly's view of federal regulation, "newly acquired information" that would have permitted Lilly to strengthen the Cymbalta warning label about withdrawal. Thus, contrary to Lilly's legal fiction that it was forbidden under federal law

from properly warning doctors about the frequency, severity, and duration of withdrawal, there is no impossibility.

With regard to Plaintiffs' design defect claims, Lilly argues that: (1) Plaintiffs allege Lilly should have redesigned Cymbalta to make it safer; (2) Lilly was forbidden from unilaterally making changes to the design of Cymbalta after the FDA approved Cymbalta; and (3) thus, Plaintiffs' design defect claims are preempted. This argument also has two flaws.

First, Plaintiffs' claims are not based on an allegation that Lilly should have redesigned Cymbalta after the FDA approved it. Rather, Plaintiffs allege that Lilly's negligence in designing Cymbalta occurred before Cymbalta was ever approved. Whether Lilly could have redesigned Cymbalta post-approval is not relevant. The only issue is whether, *before* Lilly sought FDA approval for Cymbalta, it acted negligently designing the Cymbalta capsule and dosing regimen. And, courts routinely hold that there is "no physical impossibility between complying with a state law duty to exercise reasonable care in the process leading up to placing a drug on the market and complying with the federal government's process for approving drugs." *Wimbush v. Wyeth*, 619 F.3d 632, 643 (6th Cir. 2010).

Second, Lilly ignores black letter New Hampshire law that a design defect can be cured through a proper warning about that defect. *Mut. Pharm. Co., Inc. v. Bartlett ("Bartlett")*, 133 S. Ct. 2466, 2474 (2013) ("The New Hampshire Supreme Court has recognized that this [design defect] duty can be satisfied either by changing a drug's design or by changing its labeling."). Thus, even if Lilly were forbidden by federal law in making unilateral design changes to the Cymbalta capsule, Lilly could have met its obligations under New Hampshire law by warning about that defect. And, as addressed below, nothing prevented Lilly from warning patients and doctors about the alleged design defect post-approval. There is no impossibility.

The Court should deny Lilly's Motion for Judgment on the Pleadings. Lilly simply has not

carried its "demanding" burden of establishing that compliance with New Hampshire law clearly conflicts with federal law. Thus, there is no preemption.

BACKGROUND

I. Allegations in the Complaint

This lawsuit centers on a phenomenon called "withdrawal"—the physical and mental effects patients suffer upon discontinuing Cymbalta, a selective–norepinephrine reuptake inhibitor ("SNRI"). (Compl. ¶ 10.) The physical effects patients experience upon stopping Cymbalta mirror those that drug addicts experience when they stop a narcotic: dizziness, headaches, nausea, diarrhea, excessive sweating, sensory disturbances, nightmares, and insomnia. (*Id.* ¶ 23.) However, in addition to these "typical" withdrawal effects, patients stopping Cymbalta also experience side effects that are unique to antidepressants: electric shock sensations in the brain, loss of motor functions, seizures, extreme mood swings, depression (even if the patient never previously suffered from depression), emotional outbursts, and suicidal behavior/attempts. (*Id.*)

The exact mechanism of withdrawal is unknown. However, it is widely accepted that the frequency and severity of an antidepressant's withdrawal risk is in large part associated with the drug's half-life, i.e., the amount of time for half of a drug to leave a patient's system. (*Id.* ¶¶ 15, 18.) Essentially, the shorter a drug's half-life, the faster the drug leaves the patient's body. (*Id.*) This rapid depletion, in turn, leads to more pronounced withdrawal symptoms. (*Id.*)

Much of the research about the relationship between half-life and withdrawal was conducted by Lilly as part of Lilly's efforts to bolster sales of the antidepressant Prozac in the 1990s. (*Id.* ¶ 17.) Lilly wanted to position Prozac as being superior to its competitors Zoloft and Paxil by marketing Prozac's longer half-life and superior withdrawal profile. (*Id.*) Prozac has a half-life of approximately seven days. (*Id.* ¶ 15.) Zoloft's is twenty-six hours and Paxil's is twenty-one hours. Lilly sponsored clinical trials designed to measure antidepressant withdrawal in Prozac, Paxil, and

Zoloft, and published these studies in medical journals. (*Id.* ¶ 17.) The articles espoused Prozac's superior withdrawal risk, crediting Prozac's long half-life. (*Id.*)

When it came to Cymbalta, Lilly had a problem. The half-life for Cymbalta is twelve hours—half the length of Paxil or Zoloft. (*Id.* ¶ 15.) Moreover, a pooled analysis of Cymbalta clinical trials conducted in 2005, *after* Cymbalta's approval, showed that between 44.3% and 50% of patients who stopped taking Cymbalta spontaneously[1] reported withdrawal symptoms. (*Id.* ¶ 21; *see* David G. Perahia et al., *Symptoms Following Abrupt Discontinuation of Duloxetine Treatment in Patients with Major Depressive Disorder*, 89 J. AFFECTIVE DISORDERS 207, 208 (2005) ("Perahia Article"), Exh. A.) Of these, 50.6% were moderate, 9.6% were severe, and 53.7% remained unresolved after two-weeks. (Perahia Article at 208-09.)

Plaintiffs' allegations are not limited to the Cymbalta label, however, but contemplate a failure to warn about the frequency, severity, and duration of withdrawal in all marketing, promotion, *and* labeling. (*See* Compl. ¶¶ 25, 26 39 66 80 82(b), 82(d), 82(e).) Notwithstanding, despite having clear knowledge of Cymbalta's risks of withdrawal, Lilly did not adequately warn about this risk in its labeling. The Cymbalta label as of 2012 stated:

> Discontinuation symptoms have been systematically evaluated in patients taking duloxetine. Following abrupt or tapered discontinuation in placebo-controlled clinical trials, the following symptoms occurred at 1% or greater and at a significantly higher rate in duloxetine-treated patients compared to those discontinuing from placebo: dizziness, nausea, headache, paresthesia, fatigue, vomiting, irritability, insomnia, diarrhea, anxiety, and hyperhidrosis. . . .
>
> During marketing of other SSRIs and SNRIs (Serotonin and Norepinephrine Reuptake Inhibitors), there have been spontaneous reports of adverse events occurring upon discontinuation of these drugs, particularly when abrupt, including the following: dysphoric mood, irritability, agitation, dizziness, sensory disturbances (e.g. paresthesias such as electric shock sensations), anxiety, confusion, headache, lethargy, emotional liability, insomnia, hypomania, tinnitus, and seizures. Although

[1] Use of the word "spontaneously" is deliberate. Lilly researchers did not use a systematic checklist for measuring withdrawal symptoms during the trials, but instead relied on volunteered reports from participants. Lilly researchers acknowledge that use of a symptom check list would have resulted in an increased incidence rate.

> these events are generally self-limiting, some have been reported to be severe. . . .
>
> A gradual reduction in the dose rather than abrupt cessation is recommended whenever possible. If intolerable symptoms occur following a decrease in the dose or upon discontinuation of treatment, then resuming the previously prescribed dose may be considered. Subsequently, the physician may continue decreasing the dose but at a more gradual rate.

(Compl. ¶¶ 16, 20.) Plaintiffs allege that this label is materially deficient and misleading:

- The label states that "[d]iscontinuation symptoms have been systematically evaluated in patients taking duloxetine." Plaintiffs allege that this is misleading because Lilly's evaluation of withdrawal symptoms was not systematic. (*See* Compl. ¶ 82(d).) During Lilly's marketing in the 1990s about Prozac's favorable withdrawal profile, Lilly specifically sponsored clinical trials designed to systematically compare withdrawal risks between Prozac, Paxil, and Zoloft. (*Id.* ¶¶ 17, 82(d).) In those clinical trials, Lilly "systematically monitored withdrawal using a symptom checklist." (*Id.* ¶ 82(d).) However, in studying Cymbalta withdrawal—and ultimately as part of the Perahia pooled analysis in 2005—Lilly did not use the symptom checklist it created and lauded as part of its Prozac research and marketing. (*Id.* ¶¶ 17, 21, 82(d).) Had Lilly used such a list, the rate of Cymbalta withdrawal would likely have been much higher. (*Id.* ¶¶ 21, 82(d).)[2]

- Second, the label suggests that the risk of suffering from withdrawal is rare or uncommon, occurring at a rate of "1% or greater." Plaintiffs allege that this is misleading because, in fact, withdrawal reactions are common and occur within a significant percentage of individuals who attempt to discontinue Cymbalta, i.e., at least 45% to 50%. (Compl. ¶ 82(a).)

- Third, the label does not provide any accurate information about the severity of Cymbalta withdrawal, omitting the fact that, in Lilly's Cymbalta trials, between 9.6% and 17.2% suffered severe withdrawal and over 50% suffered moderate withdrawal. (*Id.* ¶¶ 82(b).) Instead, the label misleadingly states, with regard to SSRIs and SNRIs in general, that withdrawal events "are generally self-limiting," and "some have been reported to be severe." (*Id.* ¶ 16.) This glosses over Cymbalta-specific risks. (*Id.*)

- The warning label does not discuss the anticipated duration of Cymbalta withdrawal. In Lilly's Cymbalta trials, over 50% of those who suffered from withdrawal lasted longer than two weeks. Nonetheless, Lilly makes no mention of any anticipated duration, stating, instead that withdrawal events were "generally self-limiting." This falsely gives the impression that the duration of withdrawal is limited.

  The Complaint, at paragraph 82(c) cites to and discusses the European label—which was

[2] Indeed, as Dr. Michael Detke, the global Medical Director of Prozac and Cymbalta in 2008, stated: "If you use an elicited scale, you'll see higher rates. This WILL end up in the label." *Hexum v. Eli Lilly and Co.*, 13-cv-2701-SVW-MAN, slip op. at 13 (June 19, 2015), attached as Exh. E. Lilly knew that use of a checklist or an "elicited scale" would lead to higher rates that would end up in the label. Lilly deliberately elected not to use them.

approved after the Cymbalta label in the United States. In the European label, it states that "[i]n clinical trials adverse events seen on abrupt treatment discontinuation occurred in approximately 45% of patients treated with Cymbalta[.]" (*See* European Medicines Agency, Summary of Product Characteristics (Cymbalta), at 6 (June 24, 2009), *available at* http://www.ema.europa.eu /docs/en_GB/document_library/EPAR_-_Product_Information/human/000572/ WC500036781.pdf, Exh. D.) The European label indicates that withdrawal reactions can occur "in patients who have inadvertently missed a dose." (*Id.*) The U.S. label does not discuss missing doses. The European label warns that withdrawal reactions "may be prolonged (2-3 months or more)." (*Id.*) Nowhere in the U.S. label is there a warning about duration. Finally, the European label provides instructions on how to taper, stating that Cymbalta "should be gradually tapered when discontinuing treatment over a period of no less than 2 weeks." (*Id.*) Again, the U.S. label makes no mention of how long Cymbalta should be tapered.

In addition to a failure-to-warn theory, Plaintiffs also allege that the drug is defectively designed. (*Id.* ¶¶ 19, 24.) Specifically, Cymbalta comes in 20mg, 30 mg, or 60 mg capsules. (*Id.*) Due to the short half-life of Cymbalta, the drug must be dispensed in an enteric-coated (delayed release) capsule. (*See id.* ¶ 19.) And, to ensure that the enteric coating of the Cymbalta capsule is not compromised, the Cymbalta label directs patients that the Cymbalta capsule is to "be swallowed whole and should not be chewed or crushed, nor should the contents be sprinkled on food or mixed with liquids." (*Id.* ¶¶ 19, 48.) Thus, unlike other medications which are manufactured as scored tablets that can be easily divided to create smaller doses, the smallest possible dose for Cymbalta is 20 mg, swallowed whole. (*Id.* ¶ 19.) In the context of withdrawal, this poses a serious problem. The Cymbalta label recommends tapering off the medication gradually, but practically, the patient will eventually have to quit taking Cymbalta at a 20 mg dose, without any further tapering. Thus, the actual design of the Cymbalta pill prevents the gradual tapering needed to discontinue

Cymbalta. (*Id.*) Had Lilly developed smaller doses, i.e., tapering doses, or designed the Cymbalta capsule in a way that allowed a gradual reduction of dose below 20 mg, patients would have been better able to gradually discontinue Cymbalta. (*Id.*)

II. Case History

The Complaint was filed on December 3, 2014. (Dkt. 1.) Lilly answered on January 6, 2015. (Dkt. 8.) On February 2, 2015, the parties conducted their Fed. R. Civ. P. 26(f) conference to discuss a case management plan. (*See* Dkt. 12 at 1.) During the meeting, and as reflected in the parties' Joint Discovery Plan, Lilly did not indicate any intention to raise a preemption affirmative defense. (*Id.* at 2.)

This lawsuit is one of hundreds filed around the country alleging personal injuries resulting from discontinuing Cymbalta. One case is set for trial on August 4, 2015 and another for August 11, 2015 in the Central District of California. *See Hexum v. Eli Lilly and Co.*, 13-cv-2701-SVW-MAN, slip op. at 25-26 (June 19, 2015) (denying summary judgment and setting trial date); *Herrera v. Eli Lilly and Co.*, 13-cv-2702-SVW-MAN, slip op. at 23 (June 19, 2015) (same). In these two cases, which have been pending since April 17, 2013, Lilly never raised any preemption challenges. Two other cases are scheduled to be tried together starting August 24, 2015 in the Eastern District of Virginia. *Hagan-Brown v. Eli Lilly and Co.*, 14-cv-01614-AJT-JFA (E.D. Va.); *Ali v. Eli Lilly and Co.*, 14-cv-01614-AJT-JFA (E.D. Va.). The only Court to rule on any preemption issues related to Cymbalta withdrawal, albeit in a different context, rejected the challenge. *See Saavedra v. Eli Lily & Co.*, No. 2:12-CV-9366-SVW-MAN, 2013 WL 6345442, at *7 (C.D. Cal. Feb. 26, 2013).

Concurrently with this opposition, Plaintiffs are filing a motion to amend, which seeks to update the Complaint with factual allegations tethered to the significant discovery that has been completed in related Cymbalta withdrawal cases since this case was filed.

ARGUMENT

I. Prescription Drug Preemption Primer: The Legal Landscape

Lilly's Motion for Judgment on the Pleadings focuses on federal preemption. Federal preemption is "an affirmative defense upon which the defendants bear the burden of proof[.]'" *Bruesewitz v. Wyeth LLC*, 131 S. Ct. 1068, 1087, n.2 (2011) (quoting *Fifth Third Bank ex rel. Trust Officer v. CSX Corp.*, 415 F.3d 741, 745 (7th Cir. 2005)). Federal preemption derives from the Supremacy Clause of the United States Constitution and contemplates that federal law and agency regulation may, under certain circumstances, expressly or impliedly invalidate the enforcement of state law. *Crosby v. Nat'l Foreign Trade Council*, 530 U.S. 363, 372 (2000).

The United States Supreme Court has repeatedly recognized, however, that there is a "basic presumption *against* preemption" because preemption upsets the balance of power between the federal government and the states as independent sovereigns." *Bates*, 544 U.S. at 449 (emphasis added); *see Altria Grp., Inc. v. Good*, 555 U.S. 70, 77 (2008); *Philip Morris Inc. v. Harshbarger*, 122 F.3d 58, 68 (1st Cir. 1997). This is particularly true when a defendant claims that federal law bars state action in areas traditionally regulated by the state, such as products liability. *See Medtronic, Inc. v. Lohr*, 518 U.S. 470, 474-75 (1996). To succeed on preemption, the defendant must overcome this basic presumption, which is why, according to the Supreme Court, it is a "demanding defense[,]" *Levine*, 555 U.S. at 566; *Geier*, 529 U.S. at 885.

Until the early 2000s, prescription drug companies rarely invoked conflict preemption and, "when they did, it rarely succeeded." *Mason v. SmithKline Beecham Corp.*, 596 F.3d 387, 391 (7th Cir. 2010) (citing examples). In 2001, however, the pharmaceutical industry and the FDA teamed-up "in an attempt to bolster the drug manufacturers' preemption defense" and the FDA issued new regulations seeking to insulate pharmaceutical companies from tort liability. *Id.* This caused courts to be "inundated with preemption motions in prescription drug cases." *Id.* Drug companies argued

that the FDA's approval of a drug pursuant to the Food and Drug Cosmetic Act ("FDCA"), 21 U.S.C. § 301, *et seq.*, meant that the drug was safe and the label sufficient. They argued that people should not be allowed to question the FDA's assessment and that, to do so, through application of state tort law, would violate the Supremacy Clause.

After nearly a decade of litigation in lower courts, the question was resolved in the watershed case *Wyeth v. Levine*, 555 U.S. 555 (2009). In *Levine*, the plaintiff was forced to have her arm amputated when a physician's assistant injected her with the anti-nausea drug Phenergan. *Id.* at 559. The plaintiff sued Wyeth, the brand name manufacturer of the drug, for negligence and failure-to-warn products liability. *Id.* The matter went to trial and a jury returned a verdict in favor of the plaintiff. *Id.* On appeal to the United States Supreme Court, Wyeth argued that the plaintiff's state law failure-to-warn and negligence claims were preempted. *Id.* at 564-65. Wyeth claimed that it was impossible for the manufacturer to comply with the duties imposed by state tort law and the labeling requirements set forth in the FDCA. *Id.* It also argued that permitting state claims to challenge the sufficiency of drug warnings would undermine the FDA's ability to regulate the drug industry. *Id.*

The Supreme Court rejected both arguments. *Id.* at 564-81. The Court held that state law claims were not an obstacle to the FDA's regulation of prescription medication, but rather, were an important *complement* to the FDCA's purpose of ensuring safety and efficacy. *See id.* at 575, 578; *Mason*, 596 F.3d at 39. Placing the burden exclusively on the FDA to regulate drugs was unrealistic since "the FDA has limited resources to monitor the 11,000 drugs on the market, and manufacturers have superior access to information about their drugs[.]" *Levine*, 555 U.S. at 578-79. The onus of ensuring that a drug label is accurate and complete rests with the drug manufacturer, not the FDA. *Id.* at 570-71. The drug manufacturer, not the FDA, "bears responsibility for the content of its label at *all times*[.]" *Id.*; *see In re Bayer Corp. Combination Aspirin Products Mktg.*

& Sales Practices Litig., 701 F. Supp. 2d 356, 370 (E.D.N.Y. 2010); *Chavez v. Blue Sky Natural Beverage Co.*, 268 F.R.D. 365, 372, 375 (N.D. Cal. 2010).

Three years after *Levine*, a sharply divided Supreme Court in *PLIVA, Inc. v. Mensing*, 131 S. Ct. 2567 (2011) carved out an exception to *Levine* for generic drug manufacturers. The Court held that, in light of the unique federal regulations applicable to generic drug manufacturers, failure-to-warn claims against the *generic* drug manufacturer were preempted. *Id.* at 2577. Unlike brand-name manufacturers, generic manufacturers cannot change the drug label—that power exclusively rests with the brand manufacturer. *Id.* at 2578; *see Dolin v. SmithKline Beecham Corp.*, 62 F. Supp. 3d 705, 715 (N.D. Ill. 2014). Thus, it would be *impossible* for a generic manufacturer to make any changes to a drug label absent FDA pre-approval. *Mensing*, 131 S. Ct. at 2577. Two years later, in *Bartlett*, 133 S. Ct. at 2470-78, the Supreme Court expanded *Mensing*'s defense for generic manufacturers to design defects. The Court concluded that "[g]iven the impossibility of redesigning sulindac, the only way for Mutual to ameliorate the drug's 'risk-utility' profile—and thus to escape liability—was to strengthen 'the presence and efficacy of [sulindac's] warning' in such a way that the warning 'avoid[ed] an unreasonable risk of harm from hidden dangers or from foreseeable uses.'" *Id.* at 2475. And, consistent with *Mensing*, failure-to-warn claims against generic manufacturers were preempted. (*Id.* at 2475-76.)

Neither *Mensing* nor *Bartlett* overturned or limited *Levine*. *See, e.g., Ray v. Allergan, Inc.*, 3:10CV136, 2012 WL 2120018, at *7 (E.D. Va. June 1, 2012). *Mensing* and *Bartlett* both turned on the particular regulations applicable to generic manufacturers. *In re Celexa & Lexapro Mktg. & Sales Practices Litig.*, 779 F.3d 34, 40 (1st Cir. 2015) (Noting that *Mensing* turned on the "differences in the federal 'drug labeling duties' that applied to generic manufacturers as compared to brand name manufacturers."). Indeed, since *Mensing* and *Bartlett*, courts have, consistent with the Supreme Court's guidance to "not find pre-emption too readily in the absence of clear evidence

of a conflict[,]" *Geier*, 529 U.S. at 885, refused to read *Mensing* and *Bartlett* expansively. *See, e.g.*, *Hunt v. McNeil Consumer Healthcare*, 6 F. Supp. 3d 694, 704 (E.D. La. 2014); *Fraser v. Wyeth, Inc.*, 992 F. Supp. 2d 68, 90 (D. Conn. 2014); *Estate of Cassel v. Alza Corp.*, No. 12-CV-771-WMC, 2014 WL 856023, at *5 (W.D. Wis. Mar. 5, 2014); *Dopson-Troutt v. Novartis Pharm. Corp.*, 975 F. Supp. 2d 1209, 1217 (M.D. Fla. 2013). Indeed, the majority opinion in *Bartlett*, in response to a dissent, clarified that "[t]he dissent is quite correct that federal law establishes no safe-harbor for drug companies[,]" but that a claim is *only* preempted when "state law imposes a duty to take such remedial measures" that "actual[ly] conflict[s] with federal law[.]" *Bartlett*, 133 S. Ct. at 2479 (quoting *Freightliner Corp. v. Myrick*, 514 U.S. 280, 287 (1995)).

Lilly cites the First Circuit's decision, *In re Celexa* as a legal framework for discussing preemption. *In re Celexa*, however, did not attempt to limit or distinguish *Levine*—nor could it. 779 F.3d at 42-43. *In re Celexa* was simply an example of the First Circuit applying *Levine* to a consumer protection claim involving an FDA-approved drug. *Id.*

II. Lilly Has Failed to Establish a Preemption Affirmative Defense against Plaintiffs' Failure-to-Warn Claims

Lilly only asserts conflict preemption, also known as impossibility preemption. (*See* Mem. in Supp. Mo. at 1.) Conflict or impossibility preemption occurs when enforcement of state law *clearly* conflicts with federal law, i.e., it is impossible to do what state law requires without also violating federal law. *Levine*, 555 U.S. at 568; *Mensing*, 131 S. at 257; *In re Celexa*, 779 F.3d at 43. The "existence of a hypothetical or potential conflict" is not enough. *Rice v. Norman Williams Co.*, 458 U.S. 654, 659 (1982). There must be "clear evidence of a conflict." *Geier*, 529 U.S. at 885.

In the context of a Rule 12 motion, however, all inferences in the Complaint must be viewed in a light most favorable to the Plaintiff. *Feliciano v. State of R.I.*, 160 F.3d 780, 788 (1st Cir. 1998). Moreover, Plaintiffs are only required to allege the elements of a cause of action and are *not* required to allege facts in anticipation of an affirmative defense. *United States v. N. Trust Co.*, 372

F.3d 886, 888 (7th Cir. 2004) (citing *Gomez v. Toledo*, 446 U.S. 635, 640 (1980)); *accord Oakes v. United States*, 400 F.3d 92, 98 (1st Cir. 2005). Since preemption is "an affirmative defense [,]" *Bruesewitz*, 131 S. Ct. at 1087, n.2, "for dismissal to be allowed on the basis of an affirmative defense, the facts establishing the defense must be clear 'on the face of the plaintiff's pleadings[.]'". *Blackstone Realty LLC v. F.D.I.C.*, 244 F.3d 193, 197 (1st Cir. 2001).

Here, Lilly bears a heavy burden in asserting a preemption defense. Lilly must establish that the allegations in the Complaint, when viewed in a light most favorable to the Plaintiffs, show that it would have been *impossible* to comply with its obligations under New Hampshire law without also *clearly* violating federal law. Absent a clear showing of such a conflict or *impossibility*, the presumption is *against* preemption, and this Court must deny Lilly's motion.

A. As a Threshold Matter, Lilly Cannot Establish Impossibility Preemption on Plaintiffs' Failure-to-Warn Claims Because Nothing Prevented Lilly from Complying with New Hampshire Law Through the Distribution of a "Dear Doctor" Letter or Through Its Promotional Activities

Plaintiffs' allege that Lilly violated New Hampshire law by failing to warn doctors and patients about the frequency, severity, and duration of withdrawal, and for failing to provide adequate instructions about how to safely discontinue Cymbalta. (Compl. ¶ 14.) Lilly argues that Plaintiffs' claims are preempted because it would have been impossible to strengthen the Cymbalta warning label about discontinuation symptoms, in compliance with New Hampshire law, without also violating federal law. (*See* Mem. in Supp. Mo. at 17-19.) This argument, as discussed below, is without merit since Lilly could have updated the Cymbalta label with stronger warnings about discontinuation, in compliance with New Hampshire law, and still complied with federal law.

Notwithstanding, as a threshold issue, Lilly has failed to explain why it could not have complied with New Hampshire law independent of changing the label. The Complaint alleges:

> Lilly's ***promotional campaigns*** have continuously failed to provide adequate instructions to users and health care professionals for stopping Cymbalta and have failed to include adequate warnings that fully and accurately inform users and health

> care professionals about the frequency, severity, and/or duration of Cymbalta withdrawal.

(Compl. ¶ 14 (emphasis added).) And, Plaintiffs also allege:

> Lilly could have relayed these instructions and warnings through the same means it utilized to promote its products, which included but ***are not limited to*** its labeling, "Dear Doctor letters," advertisements, and sales representatives.

(*Id.* ¶ 26 (emphasis added).) *The claims against Lilly are not limited to the Cymbalta label.* They contemplate multiple ways in which Lilly could have conveyed risk information to prescribers and patients in accord with the duties imposed by New Hampshire law. Absent from Lilly's Motion is any argument that Lilly was prevented from communicating stronger warnings to physicians outside the purview of the label. For example, Lilly does not argue that it was prevented from sending a "dear doctor" letter to prescribers discussing Lilly's data about Cymbalta withdrawal. To the extent that Lilly argues that a "Dear Doctor" letter also would have been prohibited by federal law, the undisputed facts indicate otherwise.[3] Moreover, Lilly makes no claim that Lilly was prevented, by federal law, from distributing reprints of the Perahia article to all physicians as part of its promotional efforts. This is dispositive since, unless Lilly can demonstrate that compliance with New Hampshire law would clearly conflict with federal law, there is no preemption. And here, Lilly does not even attempt to address the myriad of ways Lilly could have complied with New Hampshire warning requirements through its promotional activities beyond changing the warning label. This issue, by itself, is sufficient to defeat Lilly's motion.

B. Lilly Cannot Establish Impossibility Preemption on Plaintiffs' Failure-to-Warn Claims Because Nothing Prevented Lilly from Complying with New Hampshire

[3] Shortly after Cymbalta's approval, Lilly created an FDA-approved medical information letter about discontinuation symptoms that Lilly would send to select physicians about withdrawal. (*See* Exh. B.) Starting in 2006, this letter contained detailed information about the risks of withdrawal, mirroring the data contained in the Perahia article. (*See* Exh. C.) Nothing prevented Lilly, under federal law or FDA regulations, from distributing that letter to *all* doctors, apprising them of the information that had been published in 2005. *See* 21 C.F.R. § 200.5. Had Lilly taken such action, i.e., sent the FDA-approved letter to all physicians, Lilly could have discharged its duty to warn under New Hampshire law without violating federal law—independent of any issues related to the Cymbalta label. Thus, at least with regard to the letter, there is no impossibility preemption.

Law in Providing Accurate and Truthful Warnings Concerning Withdrawal

The focus of Lilly's preemption challenge centers on whether Lilly *could* have taken action to change the Cymbalta label to strengthen the withdrawal warning. At the heart of Lilly's preemption challenge is the legal fiction that, if Lilly had made changes to the Cymbalta label strengthening the discontinuation warnings without first obtaining FDA approval, it would have rendered Cymbalta a "new drug" under the Food, Drug, and Cosmetic Act ("FDCA"), and its distribution would have violated the misbranding statute.[4] *See Levine*, 555 U.S. at 570.

Under these "constraints" of federal law, Lilly argues that the only way Lilly could have made changes to the Cymbalta label without violating the misbranding law was to use the Changes Being Effected ("CBE") regulation. 21 C.F.R. § 314.70(c)(6)(iii)(A), (C); *see In re Celexa*, 779 F.3d 37. The CBE "permits a manufacturer to make certain changes to its label before receiving the agency's approval" provided the changes are based on "newly acquired information." *Levine*, 555 U.S. at 568. The Supreme Court, however, consistent with allowing state tort law to complement federal regulation, has broadly construed the phrase "newly acquired information." *Id.* In *Levine*, the drug manufacturer argued that "newly acquired information" was narrowly interpreted and it "could have changed [the drug]'s label only in response to new information that the FDA had not considered"—an identical claim made by Lilly. *Id.* The Supreme Court rejected this "cramped reading of the CBE regulation[.]" *Id*. at 570. The Supreme Court noted that "'newly acquired information' " is not limited to new data, but also encompasses 'new analyses of previously submitted data.' [citation

[4] To assert a preemption affirmative defense, the defendant must establish that compliance with state law conflicts with federal law. In *Levine*, *Mensing*, and *Bartlett*, the underlying law at issue is the misbranding statute, which forbids "[t]he introduction . . . into interstate commerce of any . . . drug . . . that is adulterated or misbranded" and the "misbranding of any drug . . . in interstate commerce." 21 U.S.C. § 331(a), (b); *see Levine*, 555 U.S. 570; *Mensing*, 131 S. Ct. at 2576; *Bartlett*, 133 S. Ct. at 2484 (J. Sotomayer dissenting). And, "misbranded" is defined in 21 U.S.C. § 321(n). In *Levine*, the Supreme Court explained, however, that "[t]he FDCA does not provide that a drug is misbranded simply because the manufacturer has altered an FDA-approved label; instead, the misbranding provision focuses on the substance of the label and, among other things, proscribes labels that fail to include "adequate warnings." *Levine*, 555 U.S. 570 (quoting 21 U.S.C. § 352(f)).

omitted] The rule accounts for the fact that risk information accumulates over time and that the same data may take on a different meaning in light of subsequent developments[.]" *Id.* at 569. The Court also criticized a narrow reading of the CBE regulation as being "premised on a more fundamental misunderstanding[.]" *Id.* at 570. The Supreme Court explained:

> Wyeth suggests that the FDA, rather than the manufacturer, bears primary responsibility for drug labeling. Yet through many amendments to the FDCA and to FDA regulations, it has remained a central premise of federal drug regulation that the manufacturer bears responsibility for the content of its label at all times. It is charged both with crafting an adequate label and with ensuring that its warnings remain adequate as long as the drug is on the market.

Id. at 570-71 (citations omitted). The Supreme Court could not have been clearer—federal regulation does *not* shield drug manufacturers from liability. The Court ultimately held that twenty adverse incident reports occurring over decades, all of which were reported to the FDA, was sufficient "new information" to allow a drug manufacturer to utilize the CBE regulation, suggesting that the bar for what constitutes "new information" was very low. *See Levine*, 555 U.S. at 571.

Within this legal framework, Lilly argues that, based on the allegations *in the Complaint*—and when viewed in a light most favorable to the Plaintiffs—Lilly could not have, as a matter of law, strengthened the Cymbalta warning label using the CBE regulation. This argument is based on a factual assertion that appears nowhere in the Complaint. Lilly baldly proclaims that "there is no dispute that Lilly provided the very same pre-approval clinical trial data concerning Cymbalta's discontinuation risk to the FDA before Cymbalta's launch." (Mem. in Supp. Mo. at 14.) Plaintiffs never alleged that all the data and information published in the November 2005 Perahia article—eighteen months *after* Cymbalta's approval—was considered by the FDA prior to the drug's initial approval. The Complaint, instead, notes that the publication of the Perahia article was in 2005 and that the Cymbalta labeling, which was approved in 2004, did not contain material information about the risks of withdrawal. (Compl. ¶¶ 12, 21.) In fact, the Complaint alleges that Lilly's misleading marketing efforts occurred post-approval. (*See id.* ¶ 13-14.) Contrary to Lilly's assertion, these

allegations, when viewed in a light most favorable to Plaintiffs, do not suggest that the information contained in the Perahia article was presented and considered by the FDA pre-approval, or that Lilly did not obtain any new information, as contemplated by *Levine*, allowing Lilly to use the CBE regulation to strengthen the withdrawal warning. And, absent an allegation by Plaintiffs that the information at issue *was* considered by the FDA, there is simply no factual support *within the Complaint* for Lilly's preemption defense.[5]

In a tacit admission that the four-corners of the Complaint do not allow Lilly to meet its "demanding" preemption burden, Lilly submits excerpts of a regulatory submission from 2003 produced in discovery in other Cymbalta withdrawal litigation. The document contains a chart listing out how many people experienced discontinuation-emergent adverse events ("DEAEs") in six clinical trials. (*See* Decl. Michael Imbroscio, Exh. E at pg. *135, CYM-00708137.) This data appears to match some of the data displayed in Table 2 of the Perahia article. (*See* Exh. A at 210). Lilly's submission shows that 44.3% of patients suffered a DEAE and the Perahia article, in discussing the first six studies reviewed as part of that analysis, also indicates 44.3% of patients experienced a DEAE. However, even if the Court considered this document—which is not appropriate in the context of a motion for judgment on the pleadings[6]—this document is not enough for Lilly to meet its "demanding" burden.

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[5] Indeed, as outlined in detail in the accompanying Motion to Amend the Complaint, filed concurrently with this opposition, there is a mountain of new information obtained by Lilly following Cymbalta's approval that would have given Lilly authority under the CBE regulation to strengthen the Cymbalta withdrawal warning.

[6] Consideration of documents not cited and not expressly relied on in the Complaint converts a motion under Rule 12(c) into a motion for summary judgment under Ruler 56. Fed. R. Civ. P. 12(d); *see Trans-Spec Truck Serv., Inc. v. Caterpillar Inc.*, 524 F.3d 315, 321 (1st Cir. 2008). The document presented in Lilly's motion is neither cited in the Complaint nor relied upon in making any of the allegations. Should the Court decide to consider the document, then Plaintiffs should be given the opportunity to submit evidence that disputes Lilly's assertions. *Id*. ("All parties must be given a reasonable opportunity to present all the material that is pertinent to the motion."). Should this Court wish to consider this document, then by reference, Plaintiffs incorporate all the documents submitted in support of the Motion to Amend filed concurrently with this opposition, and formally request leave to brief these issues in the context of a motion for summary judgment with its attendant standards.

First, the Complaint's allegations regarding why the Cymbalta label is misleading are not limited to the 44.3% incident rate observed in Table 2 of the Perahia article. For example, the Complaint alleges that the incident rate is "***at a minimum***, between 44.3% ***and 50%***" referencing additional open-label data obtained from other clinical trials described in the Perahia article. (Compl. ¶ 21 (emphasis added); *see* Perahia article, Exh. A, at 211 (Table 4).) Lilly has not submitted any evidence, nor is there any *allegation*, that the 50% discontinuation data was submitted to the FDA prior to approval. The Complaint alleges that Lilly's clinical trials "showed that, overall, between 9.6% and 17.2% of Cymbalta users suffered severe withdrawal[.]" (*Id.* ¶ 22.) Nothing in Lilly's submission discusses severity and nothing in the Complaint indicates that this information was submitted pre-approval. The Complaint also alleges that Lilly never disclosed how long withdrawal could last, citing the European label which indicates it could last 2-3 months. (*Id.* ¶ 82(c).) Again, there is no indication that such data was submitted to the FDA. Lilly boldly claims that "[t]he FDA could reasonably have decided not to include the total adverse event statistics because those numbers—the 44.3% on Cymbalta and the 23% on placebo—are not meaningful to the clinician[.]" (Mem. in Sup. Mo. at 16.) But this is precisely the type of "hypothetical or potential conflict" that is insufficient to support a preemption defense. *Rice*, 458 U.S. at 659. There is no allegation supporting this claim beyond Lilly's self-serving speculation.

Second, even if Lilly is correct that all the underlying data referenced in the Perahia article was submitted to the FDA prior to approval, the CBE regulations would still have permitted Lilly to rely on the Perahia article to make changes to the Cymbalta label. "'[N]ewly acquired information' is not limited to new data, but also encompasses 'new analyses of previously submitted data.'" *Levine*, 555 U.S. at 569. And, the Perahia analysis, even if it re-evaluated previously submitted data as part of a larger, pooled-analysis, is precisely the type of "new analysis" contemplated by the CBE regulation. Indeed, the Perahia article, after conducting its review, concludes that "[i]t is

recommended that, wherever possible, clinicians gradually reduce the dose no less than 2 weeks before discontinuation of [Cymbalta] treatment." (Perahia article, Exh. A, at 207-08.) This instruction for tapering over no less than two weeks, which *is* included in the European label, is not found in the U.S. label. That Perahia's analysis comes to this conclusion after reviewing data that Lilly claims was previously submitted to the FDA, illustrates the Supreme Court's comment that "the same data may take on a different meaning in light of subsequent developments[.]" *Levine*, 555 U.S. at 569. Moreover, the fact that Dr. Perahia is and continues to be a Lilly employee and that he made this medical recommendation after reviewing the data anew, gives force to the primary holding in *Levine*: "[I]t has remained a central premise of federal drug regulation that ***the manufacturer*** bears responsibility for the content of its label at ***all times***." *Id.* (emphasis added).

Thus, this case is markedly different than *In re Celexa*, where the First Circuit "scrutinized the complaint itself to see if it might plausibly be read as relying on 'newly acquired information' in contending that Forest could have changed its label through the CBE procedures[.]" 779 F.3d at 42. The Court, after reviewing the underlying complaint, could only find "two fleeting references" to two post-approval academic publications. *Id.* The first one did "not contain the information that plaintiffs say needs to be added to the label" and the second was "an opinion piece that simply argues that the FDA should not have approved Lexapro[.]" *Id.* This is in stark contrast to the publication cited here, which not only was published by a Lilly employee, but was on the specific issue that is the subject of the lawsuit. This publication specifically re-analyzed Lilly's clinical trial data and made *new* recommendations and conclusions about discontinuing Cymbalta.[7]

Lilly simply cannot establish that, after Perahia's analysis in 2005, it would have been prohibited by federal law from strengthening the Cymbalta warning about discontinuation. *Id.*

[7] Filed concurrently with this opposition brief is a motion to amend, which includes a proposed First Amended Complaint ("FAC"). In the proposed FAC there are numerous allegations, based on evidence produced by Lilly, that show that Lilly obtained a mountain of "newly acquired information" from new clinical trials, new analyses, and post-marketing surveillance reports.

("[T]he very idea that the FDA would bring an enforcement action against a manufacturer for strengthening a warning pursuant to the CBE regulation is difficult to accept."). *Id.* at 570. The Perahia analysis was post-approval and it constitutes "newly acquired information" sufficient to warrant a CBE change to the Cymbalta label.

III. Lilly Has Failed to Establish a Preemption Affirmative Defense against Plaintiffs' Design Defect Claim

With regard to Plaintiffs' design defect claim, Lilly also makes an impossibility preemption challenge. However, unlike Plaintiffs' failure-to-warn claims, this challenge is not predicated on whether there was sufficient "newly acquired information" to warrant a CBE label change. Instead, Lilly argues that, after Cymbalta was approved, Lilly was forbidden under the FDCA from making any unilateral changes to the design of Cymbalta and, thus, could not have complied with New Hampshire design-defect law. This argument falls flat for two reasons.

A. Lilly's Negligence with Regard to Cymbalta's Design Occurred Pre-Approval and there Is No Evidence that the FDA Would have Rejected a Request to Manufacturer Smaller "Tapering" Doses for Cymbalta

"In New Hampshire, the manufacturer is under a general duty to design his product reasonably safely for the uses which he can foresee[.]" *Bartlett*, 133 S. Ct. at 2473 (quoting *Reid v. Spadone Mach. Co.*, 119 N.H. 457, 465, 404 A.2d 1094, 1099 (1979)). Here, Plaintiffs allege that, long before Cymbalta was ever approved by the FDA, Lilly knew about the problems associated with Cymbalta's design, i.e., the design of the Cymbalta capsule makes it impossible to ingest doses below 20 mg, thus, making it impossible to safely taper below the "20 mg cliff." (Compl. ¶¶ 17, 18, 19, 24, 39(h), 48.) Plaintiffs allege that Lilly knew about this issue because of its research with Prozac. (*Id.* ¶¶ 17, 18, 19.) Lilly could have designed Cymbalta, pre-approval, in such a way so as to allow patients to gradually taper below 20 mg, i.e., by manufacturing smaller doses.

In the context of impossibility preemption, when the alleged negligence occurs *before* FDA approval, i.e., in the steps leading up to FDA approval, there is no conflict between state and federal

law. *Wimbush*, 619 F.3d at 643; *Cassel*, 2014 WL 856023, at *3-5. Nothing under federal law prevents a manufacturer, *before* FDA approval, from independently designing and seeking approval for a safer medication. In other words, Lilly could have complied with its obligations under New Hampshire law regarding designing safe products and not run afoul of any federal regulation. As the Sixth Circuit explains:

> In this case, as a general proposition, we can discern no physical impossibility between complying with a state law duty to exercise reasonable care ***in the process leading up to placing a drug on the market*** and complying with the federal government's process for approving drugs. This is not to say that such a physical impossibility could never exist, for instance if a state duty required that the manufacturer do something that the FDA forbade or vice versa. But such a situation would, we think, be ***the exception to the rule***. Thus, we are not persuaded that it is always impossible to comply with both state law duties and FDA regulations in the process leading up to FDA approval.

Wimbush, 619 F.3d at 643 (emphasis added).

Lilly's preemption challenge is exclusively focused on whether Lilly, *post-approval*, could have redesigned Cymbalta. (Mem. in Sup. of Mo. at 20-21.) And, to the extent that Lilly's liability could only be established by negligent conduct post-approval, this design defect challenge *might* have some merit. But the Complaint clearly alleges negligence and a duty to design a safe Cymbalta drug pre-approval, and nothing prevents Lilly from being held accountable for *that* conduct. This exact issue was addressed in *Cassel*, wherein the Court explained why pre-approval negligence is not preempted:

> [T]he bulk of defendants' argument is premised on a mischaracterization of plaintiffs' theory of the case. Defendants may well be right that adding a rate-control membrane to their existing Duragesic Matrix Patch post-FDA approval would have been a "major change" under 21 C.F.R. § 314.70(b) that they could not undertake unilaterally. . . [T]hat argument "would only matter if defendants' tort lies solely in failing to redesign the patch *after* FDA approval." [docket citation omitted] Plaintiff's theory here is that defendants had a duty to employ an alternative design . . . *before* FDA approval. [docket citation omitted]

Cassel, 2014 WL 856023, at *5-6. Here, as in *Cassel*, there is no evidence (and Lilly has not even argued) that Lilly would have been prevented by federal law or the FDA from proposing a safer

design of Cymbalta in its original New Drug Application.

Bartlett does not hold otherwise. Putting aside whether *Bartlett* applies to brand name manufacturers,[8] there is no question that *Bartlett* is limited to post-approval negligence. *See Cassel*, 2014 WL 856023, at *5-6. In *Bartlett*, the Court held that a *generic* manufacturer was prohibited by federal law from making *any* changes to the design or labeling of an already-approved drug, and thus could not comply with state tort law that required a generic manufacturer to make design or labeling changes. 133 S. Ct. at 247. However, since generic manufacturers are, by their nature, only involved with a drug *after* FDA-approval, *Bartlett* does not apply to pre-approval negligence.

Lilly might argue that *Bartlett* stands for the proposition that all design defect claims involving approved pharmaceuticals are preempted, regardless of whether those claims are against a brand name or generic manufacturer. Such an argument is not supported by *Bartlett*.

First, if the Supreme Court intended to preempt all state design defect claims, it would have said so. There is a presumption *against* preemption, *Bates*, 544 U.S. at 449, and absent a clear holding that all design-defect claims are preempted, *Bartlett* should not be broadly construed. *See Frazier v. Mylan Inc.*, 911 F. Supp. 2d 1285, 1294 (N.D. Ga. 2012).

Second, the Supreme Court in *Bartlett* specifically held that "federal law establishes no safe-harbor for drug companies" in responding to Justice Sotomayor's dissent that *Bartlett* could be interpreted as creating "an implicit and undefended assumption that federal law gives pharmaceutical companies a right to sell a federally approved drug free from common-law liability." *Bartlett*, 133 S. Ct. at 2479, 2483 (J. Sotomayor dissenting). Reading *Bartlett* as preempting all design-defect claims, even claims alleging pre-approval negligence, "would credit a criticism in which the *Bartlett* Court expressly disavowed[.]" *Cassel*, 2014 WL 856023, at *5; *see*

[8] *See Hunt*, 6 F. Supp. 3d at 703; *In re Vioxx Products Liab. Litig.*, No. MDL 1657, 2015 WL 1909859, at *10 (E.D. La. Apr. 21, 2015).

Hunt, 6 F. Supp. 3d at 704. As one federal court put it:

> [T]his Court does not interpret the *Bartlett* decision to change course and foreclose all design defect claims against prescription drug manufacturers in the absence of an express statement that it was doing so. To the contrary, because the *Bartlett* Court stated its express understanding that it was not providing a safe-harbor for drug companies, the Court declines to interpret *Bartlett* in such a way as to preempt Trahan's claims on the current limited record.

Trahan v. Sandoz, Inc., 2015 WL 2365502, at *6 n.5 (M.D. Fla. Mar. 26, 2015).

Lilly cites to three cases wherein design-defect claims against brand name manufacturers were deemed to be preempted by federal law: *Amos v. Biogen Idec Inc.*, 28 F. Supp. 3d 164, 169 (W.D.N.Y. 2014), *Yates v. Ortho-McNeil Pharm. Inc.*, No. 3:09 OE 40023, 2015 WL 66423, at *5 (N.D. Ohio Jan. 5, 2015), and *Booker v. Johnson & Johnson*, 54 F. Supp. 3d 868, 875 (N.D. Ohio 2014). These cases, however, do not apply to the claims alleged here.[9] None of these cases specifically address whether a brand name manufacturer could be liable for a design defect arising out of pre-approval negligence. *Trahan*, 2015 WL 2365502, at *6 n.5 (*Amos*, *Yates*, and *Booker*, "do not address whether the brand-name manufacturer was required to use the allegedly defective design in the first place."). These cases focus on whether a drug manufacturer can, post-approval, redesign a drug without prior FDA approval.

Plaintiffs have alleged that Lilly acted negligently in designing Cymbalta pre-approval, and there is no federal law that prohibited or conflicted with Lilly proposing smaller tapering doses to the FDA. Design-defect cases are not categorically preempted by federal law. Lilly has not carried its burden of establishing that "it is always impossible to comply with both state law duties and FDA regulations in the process leading up to FDA approval." *Wimbush*, 619 F.3d at 643.

[9] The first case, *Amos*, was decided in a single paragraph of analysis because the "plaintiffs concede that design defect claims are preempted under federal law." 28 F. Supp. 3d at 169. There was no opposition. Subsequently, the *Yates* decision relied heavily on *Amos*, relying on the fact that a "federal court in New York has already addressed the issue and has found that New York design defect tort law regarding drugs is preempted by federal law[.]" *Yates*, 2015 WL 66423, at *6. Then, the *same judge* in Yates, issued the *Booker* decision, which aimed to interpret Georgia products liability law. *Booker*, 54 F. Supp. 3d at 875. These decisions are outliers, reflecting a cascade of legal errors starting from *Amos*.

B. In Compliance with Federal Law, Lilly Could Have Changed the Cymbalta Label to Warn about Cymbalta's Design Flaw and Discharged Its Obligations under New Hampshire Law

In New Hampshire, "[t]he duty to warn is ***part of*** the general duty to design, manufacture and sell products that are reasonably safe for their foreseeable uses[.]" *Chellman v. Saab–Scania AB*, 138 N.H. 73, 78, 637 A.2d 148, 150 (1993) (emphasis added). "The New Hampshire Supreme Court has recognized that this duty can be satisfied either by changing a drug's design or by changing its labeling." *Bartlett*, 133 S. Ct. at 2474. If, as Lilly asserts, "[o]nce the FDA approves the NDA for a particular medicine, the manufacturer is prohibited from unilaterally making any" design changes, then Lilly could discharge its obligations under New Hampshire law by warning about the design issue. (Mem. in Sup. of Mo. at 20-21); *Bartlett*, 133 S. Ct. at 247. Here, Lilly could have used the CBE regulation to warn about the dosing design defect, thereby discharging its obligations under New Hampshire law. *See* 21 C.F.R. § 314.70(c)(6)(iii)(C) (CBE regulation available to "add or strengthen an instruction about dosage and administration that is intended to increase the safe use of the drug product[.]"); *Dopson-Troutt*, 975 F. Supp. 2d at 1217-18 (holding that labeling changes regarding dosing were subject to CBE changes under *Levine*).

Lilly will invariably argue that it was forbidden from using the CBE regulation to change the Cymbalta warning because any CBE change must be based on "newly acquired information" and, according to Lilly, the Complaint does not allege such new information. However, as argued above, the Complaint's reference to the Perahia article constitutes "newly acquired information" sufficient to warrant a CBE change to strengthen the Cymbalta warning, and there is no reason why that would not apply to the issues related to dosing design.

Notwithstanding, in 2007, the Division of Medication Errors and Technical Support ("DMETS") within the FDA issued a Memorandum related to Cymbalta. (*DMETS Medication Error Postmarking Safety Review*, Division of Medication Errors and Technical Support, U.S. Food

and Drug Administration (Mar. 8, 2007), *available at* http://www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm103473.pdf, attached as Exh. F.)[10] The Memorandum "identified a signal involving the opening of Cymbalta capsules prior to administration to achieve a lower dose of the drug" during "routine post-marketing surveillance[.]" (*Id.* at 1.) The Memorandum specifically identified cases wherein patients were "opening the capsules to create a dose of Cymbalta less than 20 mg in an attempt to reduce the adverse events associated with the discontinuation of Cymbalta." (*Id.* at 7.) This Memorandum, thus, identifies a safety signal about patients breaking open Cymbalta 20 mg capsules to obtain smaller doses because of withdrawal. This constitutes "new evidence" obtained from "reports of adverse events." 21 C.F.R. § 314.3(b). After 2007, Lilly could have utilized the CBE regulation to update the Cymbalta label with a warning about the design flaw with Cymbalta, discharging its obligations under New Hampshire law. There is "no evidence, let alone clear evidence, to suggest that the FDA would have rejected warnings reflecting a different dosing regimen." *Dopson-Troutt*, 975 F. Supp. 2d 1218. There is no preemption.

CONCLUSION

For the foregoing reasons, Lilly has failed to establish that compliance with New Hampshire tort law clearly conflicted with federal law. Plaintiffs have shown that Lilly could have avoided liability under New Hampshire and still fully complied with its federal obligations. There is no preemption. Lilly's Motion for Judgment on the Pleadings should be DENIED.

[10] Lilly submitted an FDA document (produced in discovery) to this Court as part of its motion. As stated above, Plaintiffs believe this is improper in a Rule 12(c) motion. Notwithstanding, should the Court elect to consider Lilly's FDA document, Plaintiffs should be allowed to submit this FDA Memorandum which, unlike Lilly's document, is publically available on the FDA website.

Dated: June 30, 2015

Respectfully submitted,

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CERTIFICATE OF SERVICE

I, R. Brent Wisner, hereby certify that, on June 30, 2015, I electronically filed Plaintiffs' **OPPOSITION TO DEFENDANT ELI LILLY'S MOTION FOR JUDGMENT ON THE PLEADINGS UNDER FED. R. CIV. P. 12(c)** with the Clerk for the United States District Court for the District of New Hampshire using the CM/ECF system, which shall send electronic notification to counsel of record.

/s/ R. Brent Wisner
R. Brent Wisner